

DETERMINATION OF TELMISARTAN AND FORCED DEGRADATION BEHAVIOR BY RP-HPLC IN TABLET DOSAGE FORM

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ABSTRACT:

A simple, rapid, precise, sensitive and reproducible reverse phase high performance liquid chromatographic (RP-HPLC) method for determination of Telmisartan (TELM) in tablet dosage form was developed and validated. Chromatographic separation was achieved on a 250 × 4.6 mm, 5μ, Waters symmetry column in gradient mode, with mobile phase consisting of a mixture of solution (10 mM potassium dihydrogen phosphate, pH 3.5 ± 0.01): acetonitrile (64:40) was used. The quantitation performed at flow rate of 1.0 mL/min at 230 nm and run time was 12 min. The analytical method was validated as per ICH guideline for linearity, accuracy, precision, specificity, limit of detection, limit of quantification, robustness and stability and method can be extended to the analysis of TELM in tablet formulations. The relative standard deviation values for precision was less than 2%, and % recovery was greater than 98% for TELM. The drug undergoes oxidative degradation, thermal degradation and in alkali medium.

Keyword: TELM, RP-HPLC, Validation, Specificity

1. Introduction:

Telmisartan (TELM) chemically described as 4[(1,4-dimethyl-2-propyl (2,6-bi-1H-benzimidazol]-1-yl)methyl][1,1-biphenyl]-2-carboxylic acid (Figure 1) is a potent, long-lasting, nonpeptide antagonist of the angiotensin II (AT1) receptor that is indicated for the treatment of essential hypertension. It selectively and insurmountably inhibits stimulation of the AT1 receptor by angiotensin II without affecting other receptor systems involved in cardiovascular regulation. In clinical studies, TELM shows comparable antihypertensive activity to other major antihypertensive classes, such as angiotensin converting enzyme (ACE) inhibitors, beta-blockers and calcium antagonists^{1,2}.

A novel formulation commercially available in TELM, benefits from the complementary modes of action of long-lasting angiotensin receptor. This provides powerful efficacy for day long control of BP and has proven evidence in cardiovascular (CV) outcomes of TELM.

Literature review revealed that there are various methods for determination of TELM, individually and in combination with other drugs. A variety of analytical methods for estimation of TELM are previously reported. The majority of methods reported are liquid chromatography coupled to UV, tandem mass spectrometry or mass

spectrometry detection but some determinations were also performed by thin layer, ratio derivative spectrophotometry and spectrofluorimetry. Individually, TELM is estimated by LC-MS³, LC-tandem MS^{4, 5}. The majority of methods reported are liquid chromatography in which TELM was estimated simultaneously with hydrochlorothiazide^{6, 7, 8}, with ramipril^{9, 10}, with AmLodipine¹¹. Some three components are also reported along with TELM such as, Column Switching LC with fluorescence detection¹². Some HPTLC methods are also reported for estimation of TELM along with other drugs^{13, 14, 15}. None of these analytical procedures has been described as a stability-indicating method for analysis of TELM in the presence of its degradation products.

Stress testing carried out to elucidate the inherent stability characteristic of the active substances and forms an important part of the API and drug product development. It suggests that degradation products that are formed under a variety of conditions should be identified and degradation pathways be established. The purpose of stress testing is to provide evidence on how the quality of drug substance varies with time under the effect of varieties of environmental factors such as acidic/alkaline medium, temperature, humidity, light and presence of oxygen. An ideal stability-indicating method is one that quantifies

the drug and also resolves its degradation products¹⁴.

The aim of present work is to develop a simple, specific, sensitive, accurate and stability indicating HPLC analytical procedure for the analysis of TELM in tablet dosage form in the presence of its degradation products and related impurities as per ICH guideline¹⁵.

2. Experimental:

a. Chemicals: TELM (99.4%) was obtained from Cipla Pharmaceutical Ltd, Mumbai, India, as gift samples. Acetonitrile (HPLC Grade), Methanol (HPLC Grade), Potassium di hydrogen phosphate (AR Grade), ortho-phosphoric acid (AR Grade) were purchased from E. Merck (India) Ltd. The 0.45- μm nylon filters were purchased from Advanced Micro Devices Pvt. Ltd. Chandigarh, India. Milli-Q water was used throughout the experiment. Tablets were purchased from Indian market containing of TELM 40mg per tablet.

b. Instruments: Analysis was performed on a chromatographic system Agilent 1200 series separation module (Japan) equipped with an auto injector (G1329A), Diode array detector SL (G1315C), Quaternary pump (G1311A) and column thermostat (G1316A). Data acquisition was made with Chemstation software. The peak purity was evaluated with DAD detector.

c. Liquid chromatographic conditions: Chromatographic conditions were obtained using a stainless steel column (Waters symmetry C₁₈ 250mm x 4.6mm 5 μm), which was maintained at 40 °C. The analytical wavelength was set at 230 nm and samples of 20 μl were injected to HPLC system. The mobile phase was Potassium dihydrogen phosphate (10mM, pH 3.0 adjusted with ortho-phosphoric acid) and acetonitrile in ratio of 60:40 (v/v) (isocratic) at a flow rate of 1mL/min. For degradation study the mobile phase was Potassium dihydrogen phosphate (10mM, pH 3.0 adjusted with ortho-phosphoric acid) and acetonitrile in ratio of 60:40 (v/v) to 70:30 (v/v) (gradient) at a flow rate of 1mL/min. The mobile phase was filtered through 0.45 μm filter and degassed for 10 minutes by sonication²⁴.

d. Standard solutions:

Stock standard solutions: An accurately weighed quantity of 40.0 mg of TELM was transferred into a 100.0 mL volumetric flask. Dissolved with 30.0 mL of methanol and diluted to required volume with mobile phase, having the concentration of 400.0 $\mu\text{g}/\text{mL}$ of TELM.

Preparation of working standard: From the standard stock solution 10.0 mL is pipette out into 100.0 mL volumetric flask and made up the

volume with mobile phase, having the concentration of 40.0 $\mu\text{g}/\text{mL}$ of TELM.

Preparation of laboratory mixture: Accurately weighed quantities of TELM (\approx 40 mg) was transferred into a 100.0 mL volumetric flask, then dissolved with 30.0 mL of methanol and diluted to required volume with mobile phase, having the concentration of 400 $\mu\text{g}/\text{mL}$ of TELM. An accurately measured 1.0 mL portion of the resultant solution was diluted to 10.0 mL with diluent to obtained a laboratory mixture having concentration similar to marketed formulation.

Sample preparation: Twenty tablets (CRESAR, Cipla Pharmaceutical Ltd.) were weighed and ground to a fine powder. An amount of powder equivalent to 40.0 mg of TELM was weighed accurately and transferred into a 100.0 mL A-grade volumetric flask containing 30.0 mL of methanol and sonicated for 30 min to effect complete dissolution of the TELM and diluted upto 100.0 mL with diluent, then the solution was filtered through 0.45 μm membrane filter and 10.0 mL of filtrate taken into 100.0 mL volumetric flask. The aliquot portion of the filtrate was further diluted to get final concentration of 40.0 $\mu\text{g}/\text{mL}$ of TELM.

e. Linearity study and Calibration curve: To study the linearity range of component, serial dilutions were made to obtained working standards in the concentration range of TELM (10-50 $\mu\text{g}/\text{mL}$). A graph was plotted as concentration of drugs versus peak area response and results found linear for analytes. From the standard stock solution, a mixed standard of working concentration was prepared containing TELM (40.0 $\mu\text{g}/\text{mL}$). The system suitability test was performed from five replicate injection of mixed standard solution²³.

f. Procedure for Forced Degradation Study:

Stability testing is an important part of the process of drug product development. The purpose of stability testing is to provide evidence of how the quality of a drug substance or drug product varies with time under a variety of environmental conditions, for example temperature, humidity, and light, and enables recommendation of storage conditions, retest periods, and shelf life to be established. The two main aspects of drug product that play an important role in shelf-life determination are assay of the active drug and the degradation products generated during stability studies. The objective of this work was to developed an analytical LC procedure which would serve as a stability-indicating method for assay of TELM drug product. Forced degradation of the drug

product was carried out under thermolytic, photolytic, acid/base hydrolytic, and oxidative stress conditions. Forced degradation of the drug products under acidic, basic, and oxidizing conditions was performed using centrifuged and filtered solution (as described in the section "Preparation of Sample Solution") containing 10 µg/mL TELM. For thermolytic and photolytic degradation, a quantity of powder equivalent to 10.0 mg TELM was exposed²⁵.

Acidic Degradation: Centrifuged sample stock solution (1.0 mL) was transferred to a 10.0 mL volumetric flask and 3.0 mL 1 M HCl was added. The mixture was left at 60 °C for 8 h in a water bath then left to equilibrate to ambient temperature, then diluted to 10.0 mL with diluent.

Alkaline Degradation: Centrifuged sample stock solution (1.0 mL) was transferred to a 10.0 mL volumetric flask and 3.0 mL 0.01 M NaOH was added. The mixture was left for 10.0 min at ambient temperature, then diluted to 10.0 mL with diluent.

Oxidative Degradation: Centrifuged sample stock solution (1.0 mL) was transferred to a 10.0 mL volumetric flask and 3.0 mL 30% H₂O₂ was added. The mixture was left for 2 hrs at ambient temperature then diluted to 10.0 mL with diluent.

Thermal Degradation: Approximately 250 mg drug product powder was left at 30°C, 40°C, 50°C for 1 month. The sample was then treated to obtain solution containing 10.0 µg/mL TELM.

UV Degradation: Approximately 250 mg drug product powder was exposed to short-wavelength UV light for 24 h. The sample was then treated to obtain solution containing 10.0 µg/mL TELM.

g. Analysis of Laboratory Mixture: In order to establish suitability of the proposed method for quantitative estimation of TELM in the pharmaceutical formulations, the method was first tried for the estimation of the component in a standard laboratory mixture of two drugs by using Equation 1 and 2.

h. Analysis of Marketed Formulation: 20.0 µl of the standard and sample are injected separately and chromatograms are generated. With peak area obtained for standard and sample, the content of TELM in each tablet was calculated using the following equation:

Amount of drug present in each tablet =

Sample area x Std. Conc. x Std. Purity x Avg. weight

Std. area x Sample conc. (1)

$$\text{Percentage label claim} = \frac{\text{Amount present}}{\text{Label claim}} \times 100 \dots\dots\dots (2)$$

i. Recovery study: Recovery studies were performed to validate the accuracy of developed method. For recovery study different concentrations (50%, 100% and 150%) of standard drug was prepared and then its recovery was analyzed.

j. Method validation: The HPLC method was validated in terms of precision, accuracy, specificity and linearity according to ICH guidelines²².

Accuracy: The accuracy of the assay method was evaluated with the recovery of the standards from excipients. Three different quantities (low, medium and high i.e. 50%, 100% and 150%) of the authentic standards were added to the placebo. The mixtures were extracted as described in section 2d, and were analyzed using the developed HPLC method.

Precision: Assay method precision was determined using nine-independent test solutions (3 concentration/3 replicates). To study precision 80%, 100% and 120% concentration was prepared and three replicate of each concentration was injected. The intermediate precision of the assay method was also evaluated using different analyst different days²⁷.

Specificity: Accurately weighed quantities of the tablets powder equivalent to about 40.0 mg of TELM was taken in a dry 50.0 mL volumetric flask. Each sample solution was stored under following different relevant small stress conditions (light, heat, acid/base hydrolysis and oxidation) for sufficient time (24 hrs) to achieve 10 to 30% degradation of the initial sample.

1. Addition of small amount of alkali solution (0.1 N NaOH).
2. Addition of small amount of acid solution (0.1 N HCl).
3. Addition of small amount of oxidative agent (3% H₂O₂).
4. Sample solution was heated 50 °C on water bath for a sufficient time
5. Sample solution was exposed 600 foot-candle of UV light for a sufficient time.

After 24 hr each treated sample was analyzed and percent labeled claims were calculated by the method using formula under estimation of TELM by proposed method.

Linearity: Solutions for linearity study were prepared as described in Section 2e. Six

replicates of each concentration were injected and results are examined and it was found that calibration curve was linear in the concentration range of 10-50 µg/mL for TELM with correlation coefficient (R^2) 0.999.

LOD and LOQ: The LOD and LOQ for analytes were estimated by SD of injecting a series of dilute solutions of known concentrations.

Ruggedness: Ruggedness was ascertained by getting the sample analyzed from different analysts and carrying out analysis on different days by proposed method.

Robustness: To determine the robustness of the method, the final experimental conditions were altered and the results were examined. The ratio of mobile phase was varied²⁹.

3. Results and Discussion:

Optimization of the chromatographic conditions:

In order to develop RP-HPLC method for cardiovascular drugs TELM in formulation. The chromatographic conditions were optimized for better resolution by using different buffers like phosphate, acetate and citrate for mobile phase preparation. After a series of screening experiments, it was concluded that Phosphate buffer (10mM Phosphate buffer pH at 3.0) gave better peak shapes than their acetate and citrate counterparts. With methanol as solvent both the peaks showed less theoretical plates and bad peak shapes, on changing to acetonitrile the peak shape improved along with theoretical plates. Further optimization experiments were carried out 30% and 40% of acetonitrile in mobile phase. The best peak shape and maximum separation was achieved with mobile phase composition consisting acetate buffer-acetonitrile (60:40 v/v). The best separation, peak symmetry and reproducibility were obtained on Waters symmetry C₁₈, 250 mm x 4.6 mm, 5 µm column compared to Hypersil ODS, C₁₈, 250 mm x 4.6 mm, 5 µm. The optimum wavelength for detecting the analytes was ascertained and found to be 230.0 nm.

Method development studies of TELM from its degradation products revealed that Pot. di hydrogen phosphate: Acetonitrile (60:40) was used which vary to (70:30 v/v) (gradient method) at a flow rate of 1.0 mL/min and a column temperature of 40°C were suitable conditions for a stability-indicating method for study of the degradation of TELM. TELM peak shape was good, with little tailing, and TELM was well resolved from its degradation products. The retention time of TELM was, typically, approximately 28.82 min and chromatographic

analysis time was than 70 min. Under the optimized conditions TELM and its degradation products were well separated.

Although the conditions used for forced degradation were attenuated to achieve degradation in the range 10–30%, this could not be achieved for thermal and photolytic degradation even after prolonged exposure. During the initial forced degradation experiments it was observed that alkaline hydrolysis of TELM was a rapid reaction the drug was extensively degraded by alkali hydrolysis, thermal and oxidative condition. Table 1 indicates the extent of degradation, and assay of TELM under the various stress conditions. Chromatograms obtained from TELM tablet solution, and solutions after thermal degradation and alkaline hydrolysis of the drug product are shown in Figure 5, 6 and Table 6.

The specificity of the HPLC method is illustrated in Figure 2 and Figure 3, where complete separation of TELM was noticed in presence of tablet excipients and its impurities produced by alkali and thermal degradation.. There were no interfering peaks of endogenous compounds observed at the retention time of the analytes.

Accuracy of the method was calculated by recovery studies at three levels by standard addition method (Table 1). The mean percentage recoveries obtained for TELM were 100.19.

Precision is the degree of repeatability of an analytical method under normal operational conditions. The system precision is a measure of the method variability that can be expected for a given analyst performing the analysis and was determined by performing 80%, 100% and 120% analyses of the working solution.

The intra-day, inter-day, analyst and instruments variability or precision data are summarized in Table 3. The R.S.D of the assay results, expressed as percentage of the label claim, was used to evaluate the method precision. The inter-day precision was also determined by assaying the tablets in triplicate per day. The results indicated the good precision of the developed method³⁰.

The developed method was applied to the analysis of TELM in tablet dosage from marketed as Cresar (Label claim 40 mg strength, Cipla Pharmaceutical Ltd.). The results of analysis are given in Table 5 and Figure 4. The contents of marketed tablet dosage form were found to be in the range of 100±2% with RSD less than 2% which indicate suitability for routine analysis of TELM in tablet dosage form.

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by

small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage. Robustness of the method was investigated under a variety of conditions including changes of pH of the mobile phase, flow rate, percentage of acetonitrile in the mobile phase. The mixed standard solution is injected in five replicates and sample solution of 100% concentration is prepared and injected in triplicate for every condition and % R.S.D. of assay was calculated for each condition. The degree of reproducibility of the results obtained as a result of small deliberate variations in the method parameters has proven that the method is robust (Table 4).

Conclusion:

In this study, a selective and validated stability-indicating RP-HPLC assay method for TELM was developed, which could separate the drug and its degradation products formed under a variety of stress conditions.

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References:

1. MS Palled, RP-HPLC determination of TELM in tablet dosage forms, *Ind. J. Pharm. Sci.*, 67 (2005) 108-110.
2. S. Kumar GV, R. Prasad Y, *Int. J. Pharmacy Pharm. Sci.*, 2 (2010) 128-131.
3. B. Chen, Y. Liang, Y. Wang, F. Deng, P. Zhou, F. Guo, L. Huang, *Anal. Chimica Acta*, 540 (2005) 367-373.
4. C. Hempen, L.G. Schwarz, U. Kunz, U. Karst, *Anal. Chimica Acta*, 560 (2006) 41-49.
5. P. Li, Y. Wang, Y. Wang, Y. Tang, J.P. Fawcett, Y. Cui, J. Gu, *J. Chromatogr. B*, 828 (2005) 126-129.
6. S.B. Wankhede, M.R. Tajne, K.R. Gupta, S.G. Wadodkar, *Ind. J. Pharm. Sci.*, 69 (2007) 298-300.
7. L.I. Bebawy, S.S. Abbas, L.A. Fattah, H.H. Refaat, *II Farmaco*, 60 (2005) 859-867.
8. T. Yan, H. Deng, Y. Guo, W. Yu, J.P. Fawcett, D. Zhang, Y. cui, J. Gu, *J. Pharm. Bio. Anal.*, 48 (2008) 1225-1229.
9. S. Jawla, K. Jeyalakshmi, T. Krishnamurthy, Y. Kumar, *Int. J. ChemTech Res.*, 2 (2010) 1625-1633.
10. A.K. Muthu, R. Sankhla, S. Gupta, A.A. Smith, R. Manavalan, *J. Appl. Chem. Res.*, 12 (2010) 43-52.
11. M.D.R. Brunetto, Y. Contreras, S. Clavijo, D. Torres, Y. Delgado, F. Ovalles, C. Ayala, M. Gallignani, J.M. Estela, V.C. Martin, *J. Pharm. Bio. Anal.*, 50 (2009) 194-199.
12. V.A. Patel, P.G. Patel, B.G. Chaudhari, N.B. Rajgor, S.G. Rathi, *Int. J. Pharm. Bio. Res.*, 1 (2010) 18-24.
13. N.R. Vekariya, M.B. Patel, G.F. Patel, R.B. Dholakiya, *J. Young Pharm.*, 1 (2009) 259-263.
14. L.V. Potale, M.C. DamLe, A.S. Khodke, K.G. Bothara, *Int. J. Pharm. Sci. Res.*, 2 (2010) 35-39.
15. J Shen, HPLC determination of TELM in human plasma and its application to a pharmacokinetic study, *Pharmazie*, 2005, 60(6), 418-20.
16. S. Bankey, G.G. Tapadiya, S.S. Saboo, S. Bindaiya, D. Jain, S.S. Khabadi, *Int. J. ChemTech Res.*, 1 (2009) 183-188.
17. A.B. Thomas, S.N. Jagdale, S.B. Dighe, R.K. Nanda, *Int. J. ChemTech Res.*, 2 (2010) 1334-1341.
18. U.P. Patil, S.V. Gandhi, M.R. Senger, V.S. Rajmane, *Int. J. ChemTech Res.*, 1 (2009) 970-973.
19. K.U. Chaudhari, P.D. Gaikwad, V.H. Bankar, S.P. Pawar, *Int. J. Pharmacy Tech.*, 2 (2010) 255-264.
20. U.P. Patil, S.V. Gandhi, M.R. Senger, V.S. Rajmane, *J. Chil. Chem. Soc.*, 55 (2010) 94-96.
21. ICH, Validation of Analytical Procedures: Methodology (Q2B). International Conference on Harmonization, IFPMA, Geneva, 1996.
22. A.G. Goodman, L.S. Gilman, in: A.G. Gilman, T.W. Rall, A.S. Nies, P. Taylor (Eds), *The pharmacological basis of Therapeutics*, 8th ed., Pergamon Press, Oxford, 1990, pp.
23. K.D.Tripathi, *Essential of medical pharmacology*, 5th ed. Jaypeebrothers medical publishers (p) ltd, New delhi, pp. 591-593.
24. G. Chatwal, S.K. Anand, *Instrumental methods of Chemical Analysis*, 5th edition, Himalaya publishing house, New Delhi, 2002, pp. 1,1-1.8, 2.566-2.570.
25. W. Kemp, *Organic Spectroscopy*, Palgrave, New York, 2005, pp. 7-10, 328-330.
26. D. A. Skoog, F. J. Holler, T.A. Nieman, *Principle of Instrumental Analysis*, 5th edition, Saunders College Publishing, 1998, pp. 778-787.
27. R. Snyder, J. Kirkland, L. Glajch, *Practical HPLC method development*, A Wiley International publication, II Ed, 1997, pp. 235,266-268,351-353.653-600.686-695.
28. A.C. Moffat, M.D. Osselton, B. Widdop, *Clarke's Analysis of Drugs and Poisons*, Pharmaceutical Press, London, 2005.
29. S.C. Sweetman, *Martindale the Complete Drug Reference*, 34th ed., Pharmaceutical Press, London, 2005, pp. 1218-1219, 1409-1410.
30. *The British Pharmacopoeia*, HMSO, London, 2009, p. 1609 – 1611.

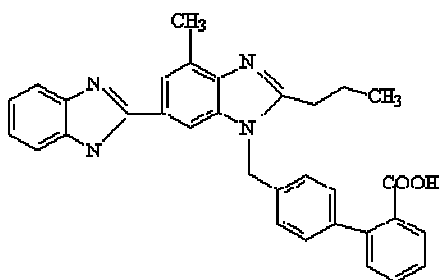


Figure 1 Structure of TELM



Figure 4 Test solution for assay



Figure 2 Alkali degradation test solution for specificity

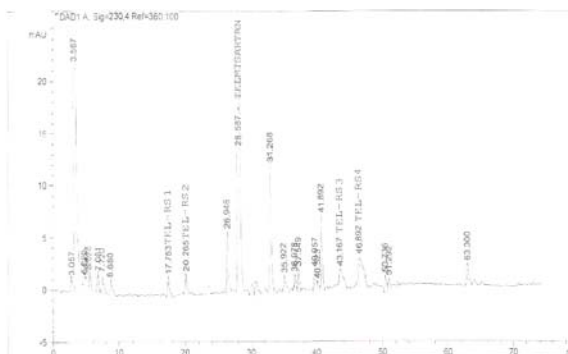


Figure 5 Thermal degradation of tab sample at 50 °C temp.



Figure 3 Thermal degradation test solution for specificity

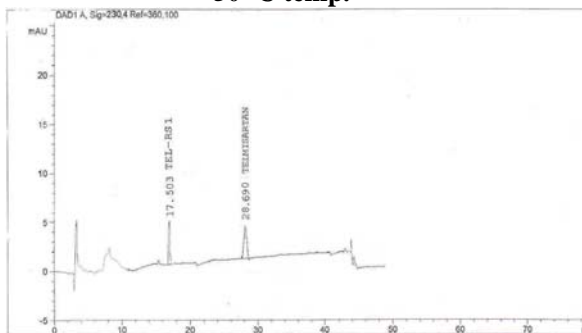


Figure 6 Alkali degradation (2 N NaOH, 24 h) of tab sample

Table 1 Results of recovery analysis of TELM

Compound	Wt. Spiked (%)	Wt. recovered (%)	Recovery (%)	RSD (%) n=3
TELM	50	49.95	99.9	0.011
	100	99.942	99.94	0.005
	150	151.122	100.748	0.003

Table 2 System suitability Parameter of TELM

Parameters	Atorvastatin
Theoretical plates	8721
Peak Height	7.56
Peak Symmetry	0.981
USP tailing	1.018
Width at half height	0.389

Table 3 Results of precision of TELM

Compound	Precision	Mean	RSD (%)
TELM	Intra day	100.55	0.007
	Inter day	100.53	0.042
	Analyst	100.56	0.007
	Instrument	100.37	0.267

Table 4 Results of robustness study of TELM

Factor	Level	Mean % assay (n=3)	RSD (%)
pH of mobile phase	3	99.5	0.209
	3.2	99.0	0.210
Flow rate (mL/min)	1	99.6	0.057
	1.3	99.3	0.209
% of Acetonitrile	30	99.1	0.307
	40	100.8	0.198

Table 5 Quantitative analysis of marketed formulation of TELM

Tablet Sample	Label Claim (mg)	Amount present (mg/tablet)	%Label Claim	%Deviation
TELM	40	39.66	99.15	-0.85

Table 6 Results of forced degradation study

Stress condition		Degradation % of TELM	% Assay
Thermal Stress	30 °C	3.16	96.84
	40 °C	7.88	92.12
	50 °C	18.64	81.36
Alkaline stress	0.1 N NaOH, 8h	8.8	91.20
	1 N NaOH, 12h	27.84	72.16
	2 N NaOH, 24h	38.29	61.71
Oxidative stress	3 %, 6 h	No Degradation	99.28
	3 %, 24 h	No Degradation	99.18
	10 %, 24 h	3.18	96.88
Acidic stress	0.1 N HCl / 8 h	No Degradation	99.28
	1 N HCl / 12 h	No Degradation	99.25
	2 N HCl / 24 h	No Degradation	99.25
	5 N HCl / 24 h	No Degradation	99.19
UV stress	1.2×10 ⁶ Lux hours	No Degradation	99.18
	6×10 ⁶ Lux hours	No Degradation	99.19